REMARKS

Status of Claims and Amendment

Upon entry of the amendment, which is respectfully requested, claims 31, 34, 35 and 37 will be amended. Claims 1-30 and 36 have been canceled. Claims 31-35 and 37-53 are all the claims pending in the application.

Claim 31 has been amended to replace "isolated or cloned" with "derived". Support for the amendment to claim 31 may be found at least at page 13, lines 9-23 of the present specification

Claims 34 and 35 have been amended to replace "selected from" with "comprising one or more of" to further define the claimed invention.

Claim 37 has been amended to change the claim dependency.

No new matter is added.

Withdrawn Objections/Rejections

1. Applicants thank the Examiner for withdrawal of the objection to Figures 4-9 and the objection to claim 34.

2. Applicants thank the Examiner for withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

Response to Rejections under 35 U.S.C. § 112, Second Paragraph for Indefiniteness

1. Indefiniteness

Claims 31-34 and 38 remain rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for reciting the term "derived." .

In response, Applicants note that the claims prior to the present amendment clearly reflects what Applicants consider to be the claimed invention. However, solely to advance prosecution of the present application, claim 31 has been amended to replace the term "derived" with "isolated or cloned." Claims 32 and 33 are definite by virtue of their dependency on claim 31. Applicants respectfully submit that the indefiniteness rejection does not apply to claims 34 and 38, as these claims do not recite "derived."

Reconsideration and withdrawal of the rejection under § 112, second paragraph, is respectfully requested.

2. Claims 34-35 and 37-38 remain rejected in part under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Office Action appears to assert that Applicants' arguments and amendment of claims to recite "SEQ ID NOs: 1, 2, and 3" is persuasive in part, but the claims are unclear as to whether the claimed sequences consist of or are subsequences of the designated SEQ ID NOs.

In response, Applicants note that the claims prior to the present amendment clearly reflects what Applicants consider to be the claimed invention. However, solely to advance prosecution of the present application, claim 34 has been amended to recite that the nucleotide molecule comprises "at least one nucleotide sequence comprising one or more of". Similarly, claim 35 has been amended to recite that the polypeptide comprises "at least one amino acid sequence comprising one or more of". Claims 37 and 38 are definite by virtue of their dependency on claims 34 and 35.

Reconsideration and withdrawal of the rejection under § 112, second paragraph, is respectfully requested.

3. Claim 37 is newly rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for being dependent on a canceled claim 36.

In response, claim 37 has been amended to be dependent on claim 35.

Accordingly, the rejection under § 112, second paragraph, is rendered moot.

Response to Rejections under 35 U.S.C. § 112, First Paragraph for Lack of Enablement

1. Claims 34-35 and 37-38 remain rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement for the scope of any/all fragments of the claimed heat shock protein providing pain relief.

The Office Action asserts that Applicants' arguments are not found to be persuasive because the specification only uses cpn 60.1, cpn 60.2 or cpn 10 so that any subsequence or sequence other than one that is 100% identical to cpn 60.1, cpn 60.2 or cpn 10 are not enabled by the specification.

In response, Applicants note that as previously argued, the structural characteristic of chaperonin 60 and chaperonin 10 are well-established in the art. (See page 2, lines 5-11 of the specification). In addition, *Mycobacterium tuberculosis* is known to produce chaperonin 60.1 (cpn 60.1), chaperonin 60.2 (cpn 60.2), and chaperonin 10 (cpn 10). (See page 2, lines 26-29 of the specification). In fact, the naming of chaperonin 60.1 is based upon its amino acid sequence identity with other known chaperonins. Id. Accordingly, chaperonin 60.2, or SEQ ID NO:4 and 3, respectively, is disclosed to exhibit 59.6% identity to the amino acid sequence of cpn 60.1 (SEQ ID NO:2), and 65.6% identity to the nucleic acid sequence of cpn 60.1 (SEQ ID NO:1). (See page 3, lines 1-2 and page 9, lines 10-14 of the specification). An assay to determine the pain relief activity of the claimed nucleotides and claimed polypeptides is provided in Examples

2 and 3 and the results are illustrated in Figures 6 and 7 to show the reduction in hyperalgesia to endotoxin (or sensitivity to pain) as expressed by the duration of paw withdrawals.

Furthermore, as disclosed at page 8 of the present specification, one skilled in the art would understand and surmise based on common technical knowledge and the disclosure in the specification, e.g., determination of the percent identity in the amino acid sequence based on the GAP program, Clustal W program, FAST pairwise alignment program, BLOSUM, or even a BLAST search algorithm, in order to make and use the claimed nucleotides having at least 66% identity to sequence (i), and the claimed polypeptides having at least 60% or more identity to sequence (i).

Accordingly, because the action of proteins is often attributed to particular domains and the full-length protein is not generally required for activity, it would be a matter of routine experimentation to test the claimed nucleotides and claimed polypeptides for their pain relief characteristics. For example, Tormay, *et al.* (Journal of Biol. Chem, 280(14): 14272-14277 (2005))[1] teach that the biological activity of *Mycobacterium tuberculosis* cpn 60 proteins resides in the individual monomers. See Tormay, page 14277, 2nd column, last full paragraph. Further, Tormay teaches structural model of cpn 60.1 was obtained by sequence alignment of *Mycobacterium tuberculosis* cpn 60.1 with GroEL using ExPASy modeling server. See page 14274, Figure 2. In this regard, Tormay teaches a three-dimensional representation of the monomer structure of the cpn 60.1 protein including apical, intermediate and equatorial domain.

[1] In accordance with M.P.E.P. 609(c), the documents cited herein in support of Applicants' remarks are being submitted as evidence to an issue raised in the Official Action, and no fee pursuant to 37 C.F.R. 1.97 or 1.98, or citation on a FORM PTO/SB/08 or PTO-1449 is believed to be necessary.

See page 14274, Figure 2. Furthermore, Tormay provides the sequence of cpn 60.1 with the domain structure outline underneath. See page 14274, Figure 2.

Furthermore, Tormay compares the cytokine-inducing activity of the recombinant cpn 60.1 domains. See Tormay, page 14274, 2nd column, 2nd full paragraph. In this regard, the full-length parent protein, the equatorial domain, and the equatorial plus intermediate domain all demonstrated the capacity to induce pro-inflammatory cytokine synthesis. See Tormay, page 14274, 2nd column, 2nd full paragraph. In most experiments the equatorial domain and the equatorial domain linked to the intermediate domain showed higher potency and efficacy than the full-length parent protein. See Tormay, page 14274, 2nd column, 2nd full paragraph. This was particularly marked with the induction of IL-1β synthesis. See Tormay, page 14274, 2nd column, 2nd full paragraph.

Thus, because the present specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, the enablement requirement of 35 U.S.C. 112 is satisfied. Further, even in the unpredictable arts, a disclosure of every operable species is not required. M.P.E.P. § 2164.03. In this regard, the Board of Patent Appeals and Interferences (BPAI) has found that one of ordinary skill in the art would understand whether a particular protein has at least 50% similarity with the claimed sequence, and that the functional assays disclosed in the specification provide sufficient guidance for one skilled in the art so that it would not require undue experimentation for one skilled in the art to "make and use" the claimed methods. *Ex parte Smith* (B.P.A.I. 2005). This is also consistent with the BPAI's recognition in *Ex parte Kubin* (B.P.A.I. 2007) that Applicants' claims reciting nucleic acids encoding at least 80% identity to the claimed amino acid sequence are enabled because that "[t]he amount of experimentation to practice the full scope of the claimed

invention might have been extensive, but it would have been routine. The techniques necessary to do so were well known to those skilled in the art."

Reconsideration and withdrawal of the rejection under § 112, first paragraph, is respectfully requested.

2. Claims 31-35 and 37-53 remain rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement for relieving pain by administering the claimed polynucleotides encoding a heat shock polypeptide.

The Office appears to rely on the same rationale as discussed above under the enablement rejection, i.e., that although the specification teaches that whole cpn 60.1, cpn 60.2 or cpn 10 polypeptides may be used to achieve the claimed pain relief, the specification does not enable any subsequence or sequence other than one that is 100% identical to cpn 60.1, cpn 60.2 or cpn 10 and retain of pain relief characteristics as claimed.

In response, Applicants respectfully disagree for the same reasons as discussed above. In addition, Applicants note that treatment using nucleotide sequences are well-known in the art through gene therapy approaches (See Lim et al, *Current Gene Therapy*, 9(1):1-8 (2009)).

Accordingly, one of ordinary skill in the art would be enabled to make the claimed polypeptide or nucleotide molecule encoding a heat shock polypeptide to provide pain relief treatment.

Reconsideration and withdrawal of the rejection under § 112, first paragraph, is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The U.S. Patent and Trademark Office is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

Tu A. Phan, Ph.D.
Registration No. 59,392

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

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